



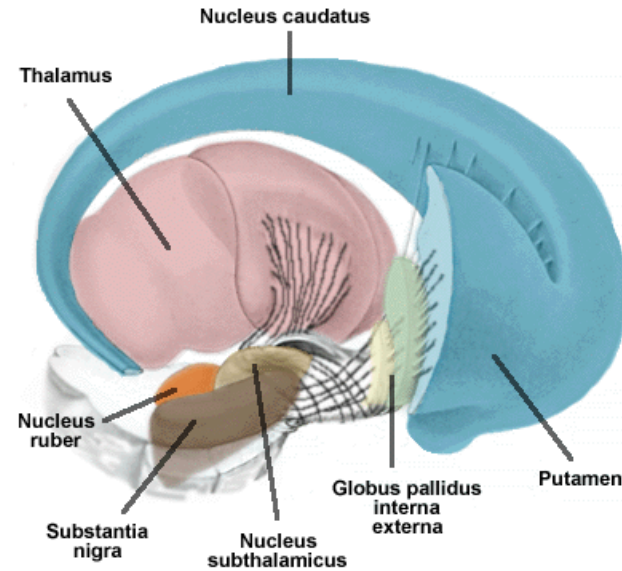
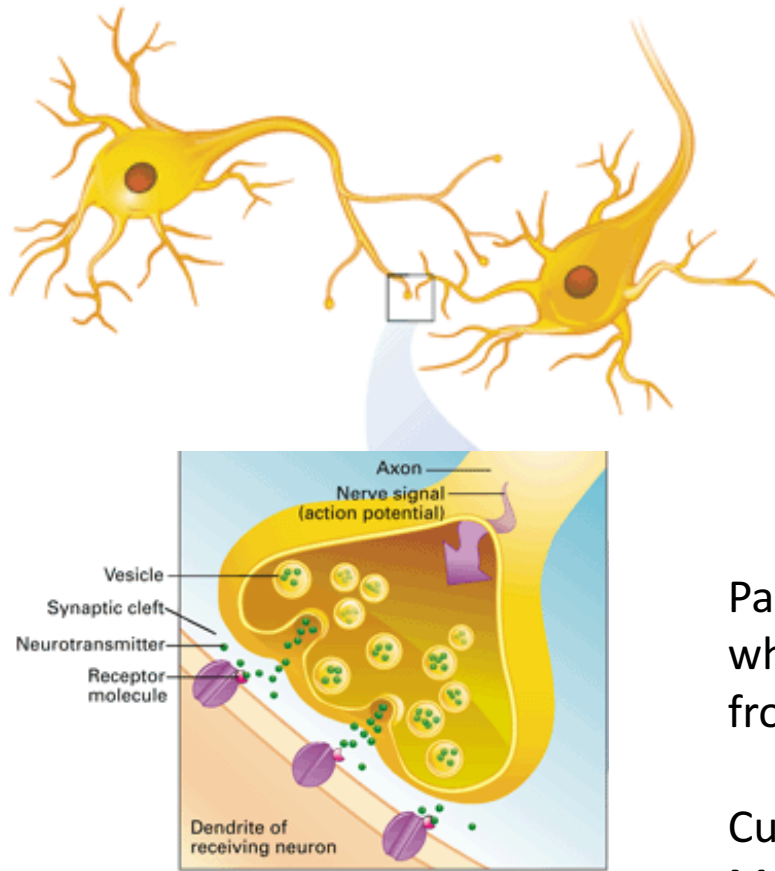
Carbon nanofiber electrode array for neurochemical monitoring

Jessica E. Koehne

NASA Ames Research Center

Moffett Field, CA

Background: Parkinson's Disease



Parkinson's disease is a neurodegenerative disorder in which patients have insufficient production of dopamine from dopaminergic cells in the substantia nigra

Current treatments include L-dopa, dopamine agonists, MAO-B inhibitors, surgery (ablation and deep brain stimulation)

Deep Brain Stimulation



Deep Brain Stimulation (DBS)

-Started in the 1960's
-Has been demonstrated to be an effective neurosurgical treatment for several pathologies including:

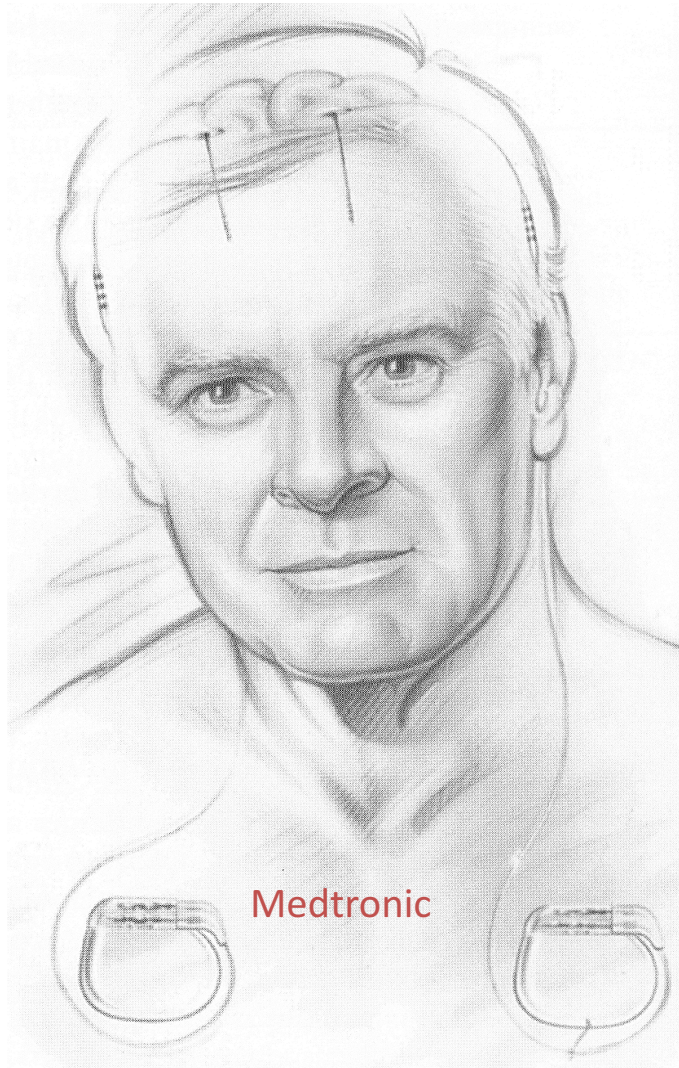
- tremor
- epilepsy
- Parkinson's disease
- depression
- Tourette syndrome
- chronic pain

How DBS Works

-Brain pacemaker, electrical impulses to different areas of the brain
-Stimulation 24/7
-**Has been shown to induce dopamine release**

Potential Improvements

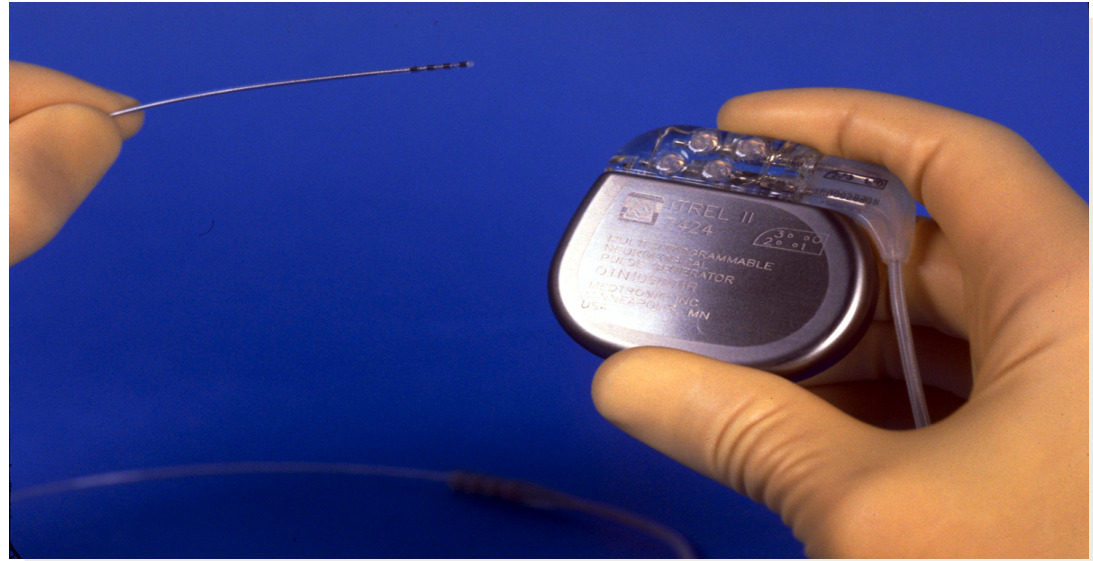
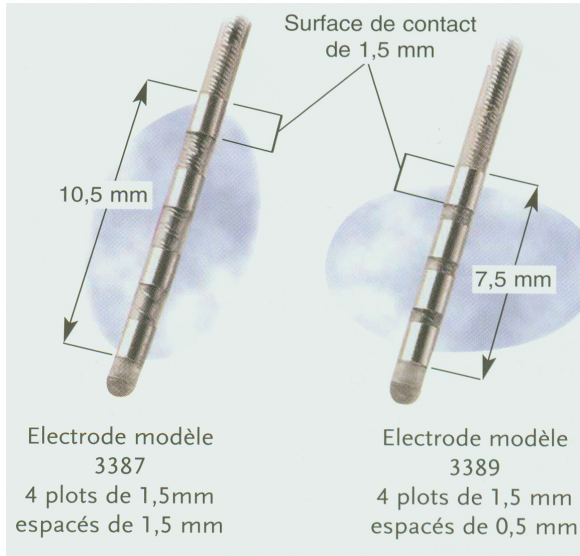
-Time consuming and difficult to program without feedback
-Want real-time monitoring of the neurochemical output



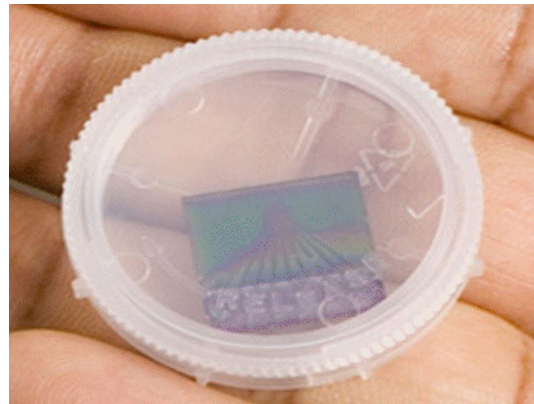
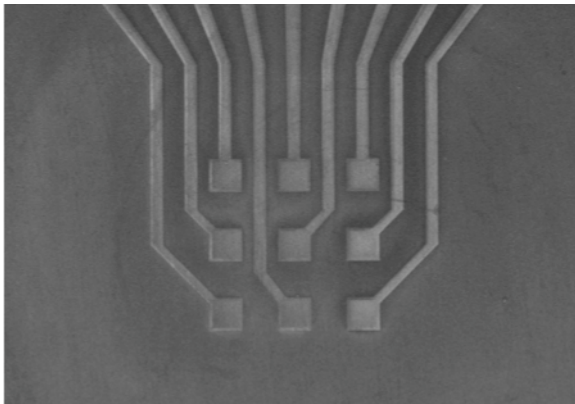
Clinical efficacy is not questioned, but mechanisms are very poorly understood

Deep Brain Stimulation Electrodes

DBS Electrodes from Medtronic



Carbon Nanofiber (CNF) Sensor



Current 3x3 CNF device does not have an optimal geometry for implantation but can be used for preliminary in vitro investigations.

Nanoelectrodes for Chemical Sensing

Nanoscale electrodes create a dramatic improvement in signal detection over traditional electrodes for small analyte concentrations

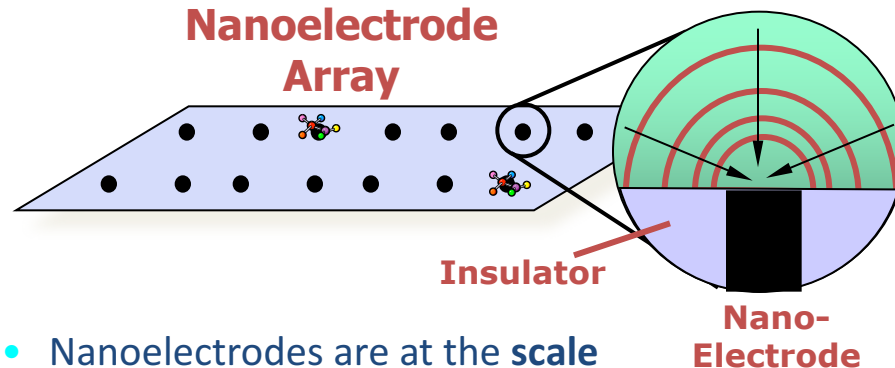
$$\text{Background: } i_n \propto C_d^0 A$$

Traditional Macroelectrode



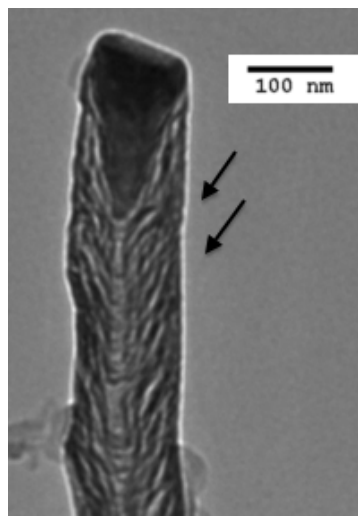
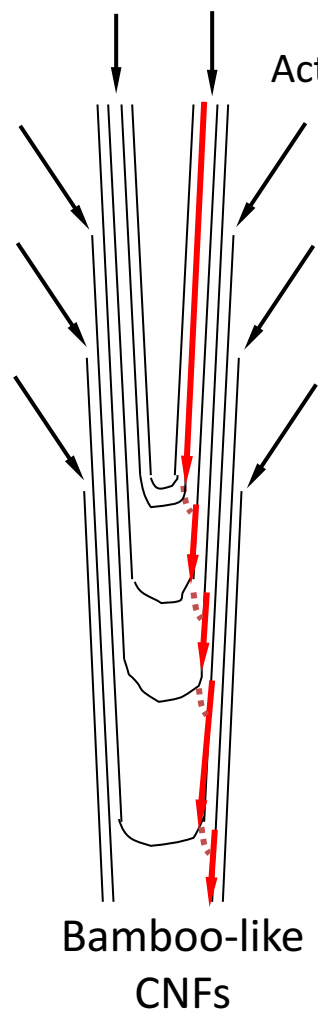
- **Scale difference** between macroelectrode and molecules is tremendous
- **Background noise** on electrode surface is therefore significant
- **Significant amount** of target molecules required

Nanoelectrode Array

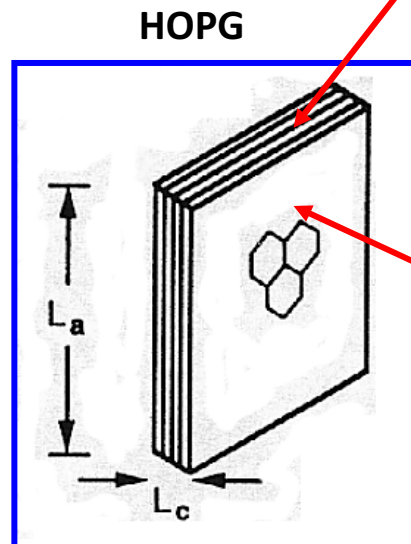


- Nanoelectrodes are at the **scale close to** molecules
- with dramatically **reduced background noise**
- Multiple electrodes results in **magnified signal** and **desired redundancy** for statistical reliability.

What are Carbon Nanofibers (CNFs)?



TEM of CNF



Edge Plane:

- (1) High electron transfer rate (~ 0.1 cm/s)
- (2) Very high specific capacitance (>60 $\mu\text{F}/\text{cm}^2$)

Basal Plane:

- (1) Low electron transfer rate ($< 10^{-7}$ cm/s)
- (2) Anomalously low capacitance (~ 1.9 $\mu\text{F}/\text{cm}^2$)

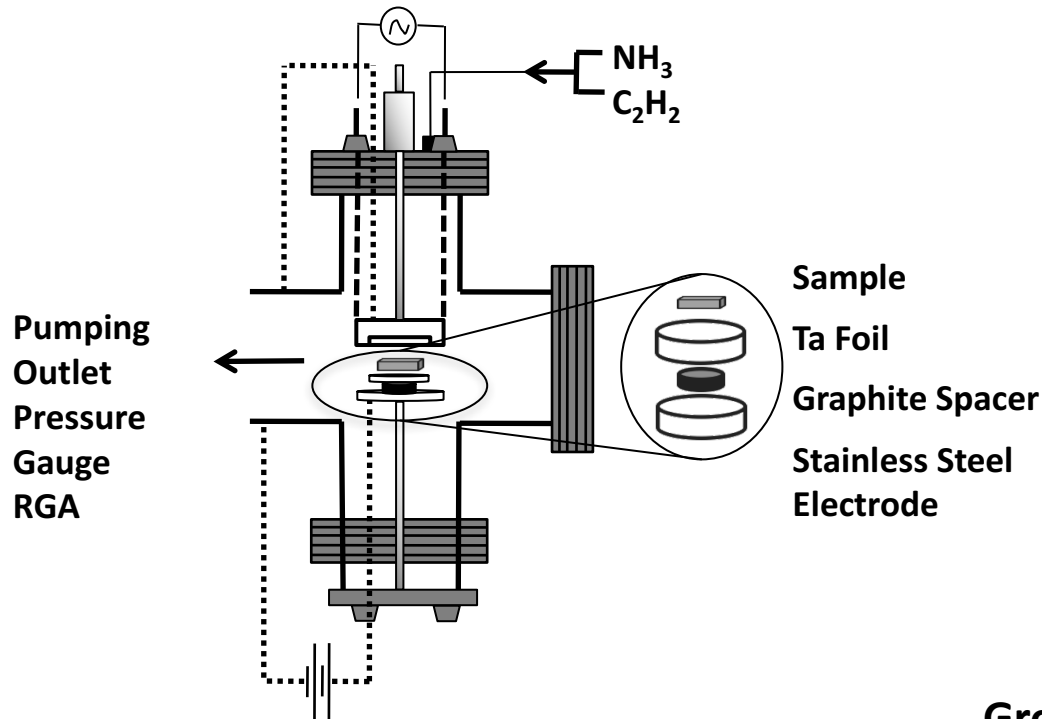
R. L. McCreery, A. J. Bard, in *Electroanalytical Chemistry*, Ed., 1991, 17, 221.

Why CNF as biosensor electrode material?

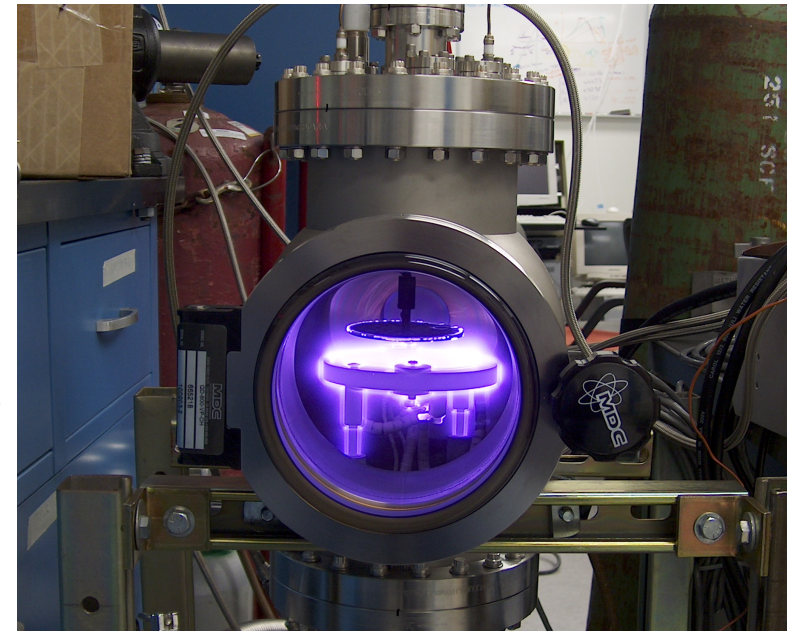
- 1) Good conductivity
- 2) Wide potential window
- 3) Many active sites for electron transfer
- 4) Easy to pattern, grow and process on silicon devices

CNF Growth by Plasma Enhanced Chemical Vapor Deposition (PECVD)

PECVD Reactor Schematic



Custom Built PECVD Reactor

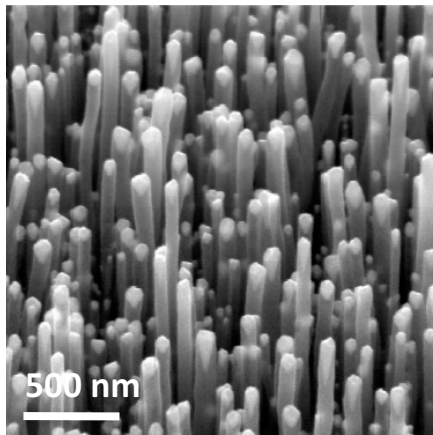


Growth Process

- Heated to 650 C
- Plasma discharge 500 W, 530 V, 0.97 A
- 150 sccm NH_3 /50 sccm C_2H_2 , 5-6 torr
- Growth rate- 1000 nm/min
- Quality is good, alignment is good

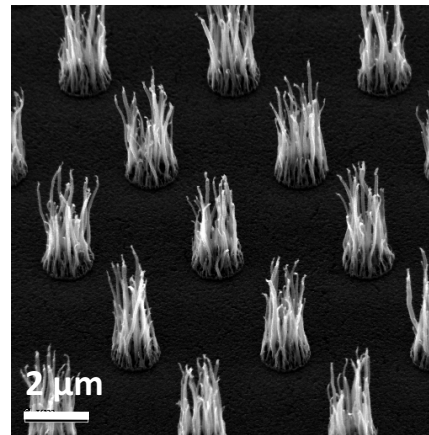
Define CNF Placement by Catalyst Placement

Continuous Layer of Catalyst

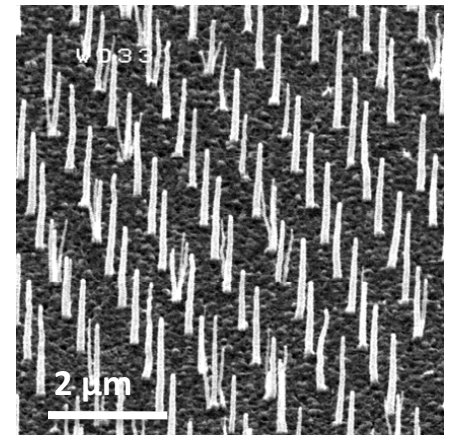


As Grown CNFs

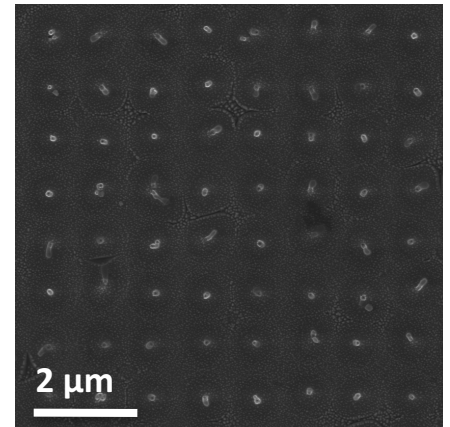
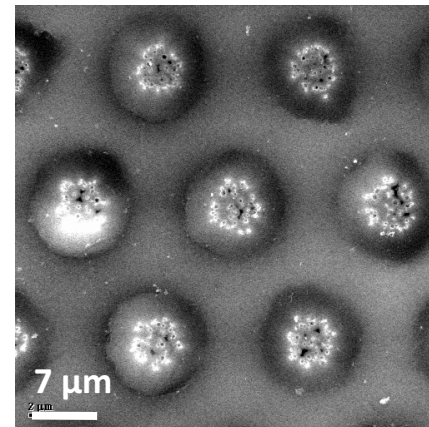
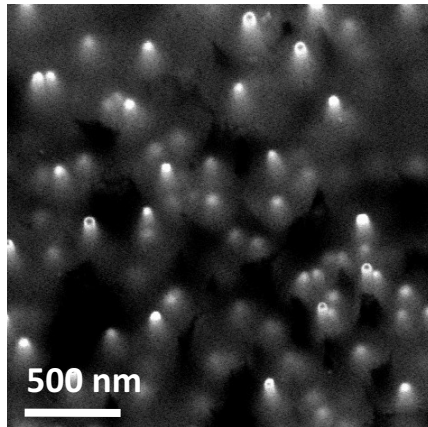
Photolithography Defined Catalyst Spots



Electron Beam Lithography Defined Catalyst Spots

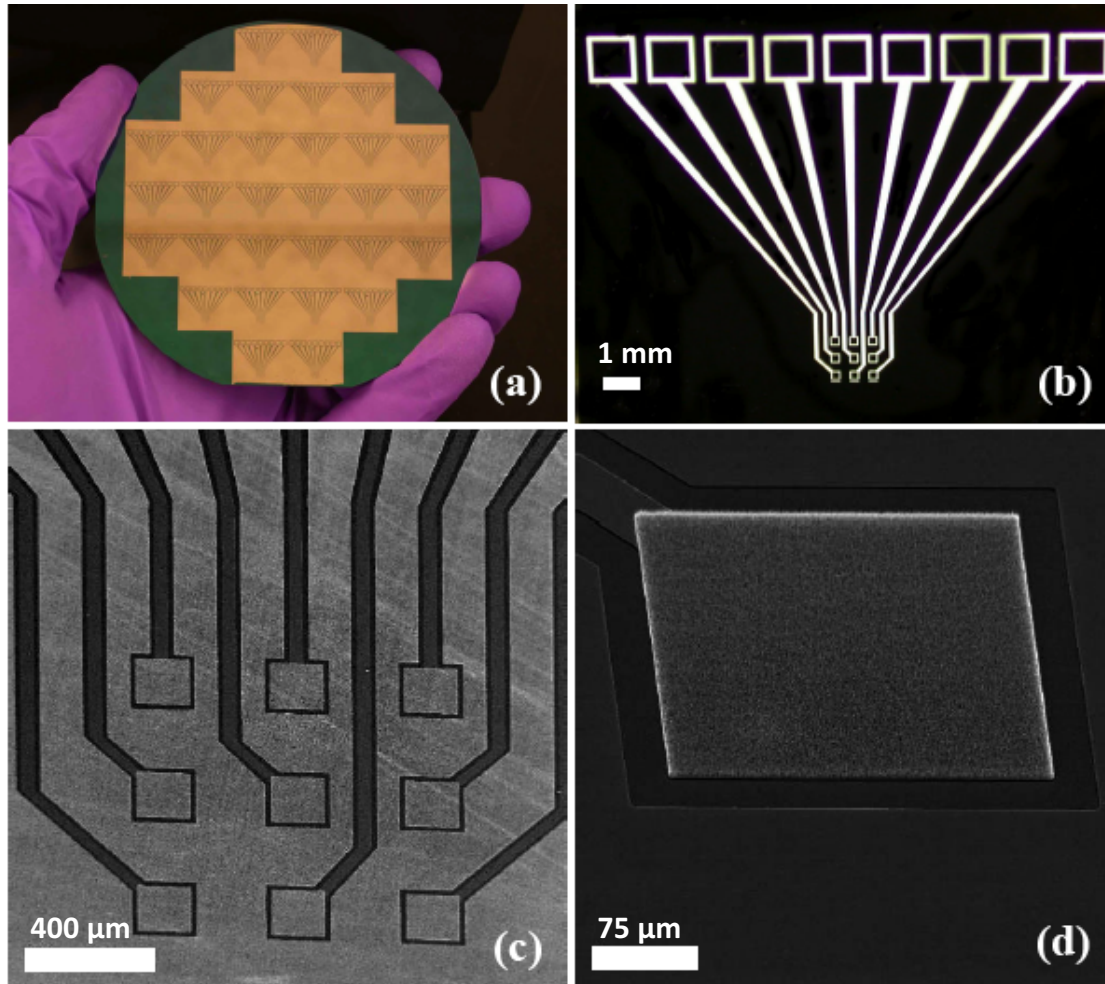


SiO₂ Encapsulated CNFs



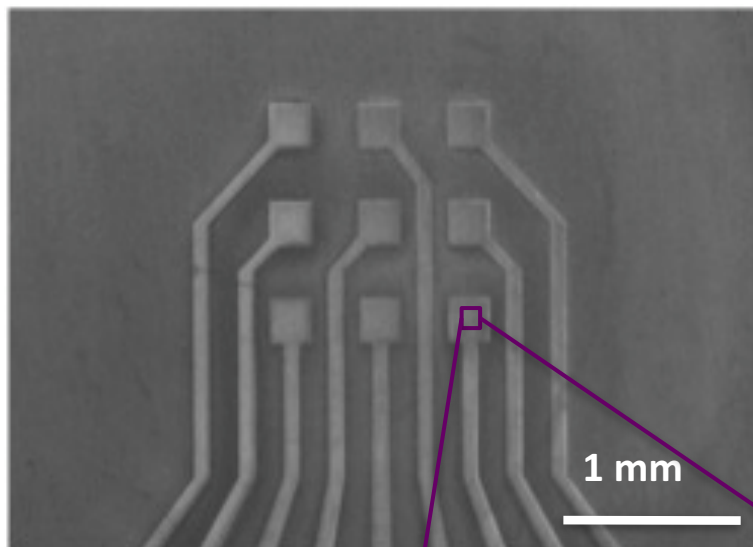
Fabrication of 3x3 Array

30 devices on
a 4" Si wafer

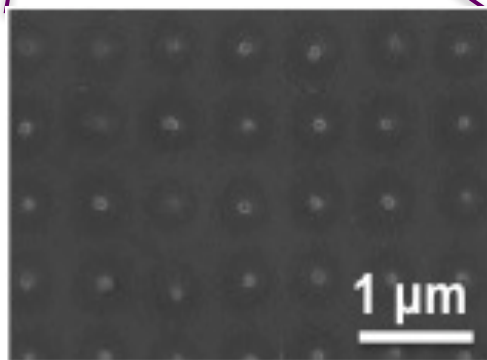


- 200 μm by 200 μm electrode dimensions
- 9 individually addressed electrodes
- potentially 9 different target molecules

Electrochemical Detection of Neurotransmitters



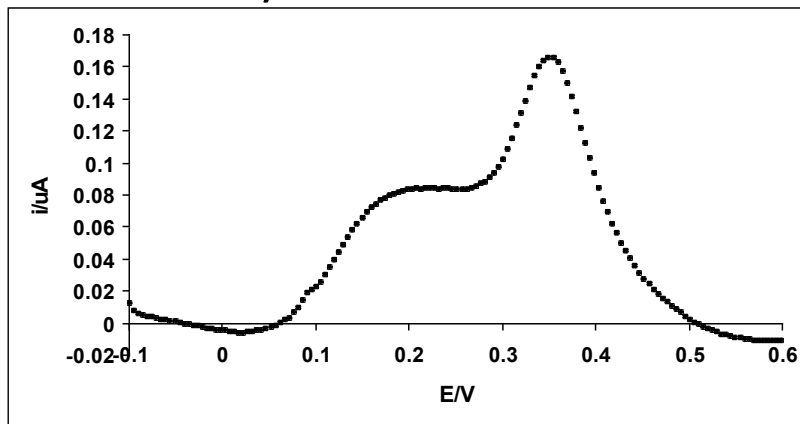
Recording Electrode:
CNFs embedded in
 SiO_2 with ultrahigh
sensitivity



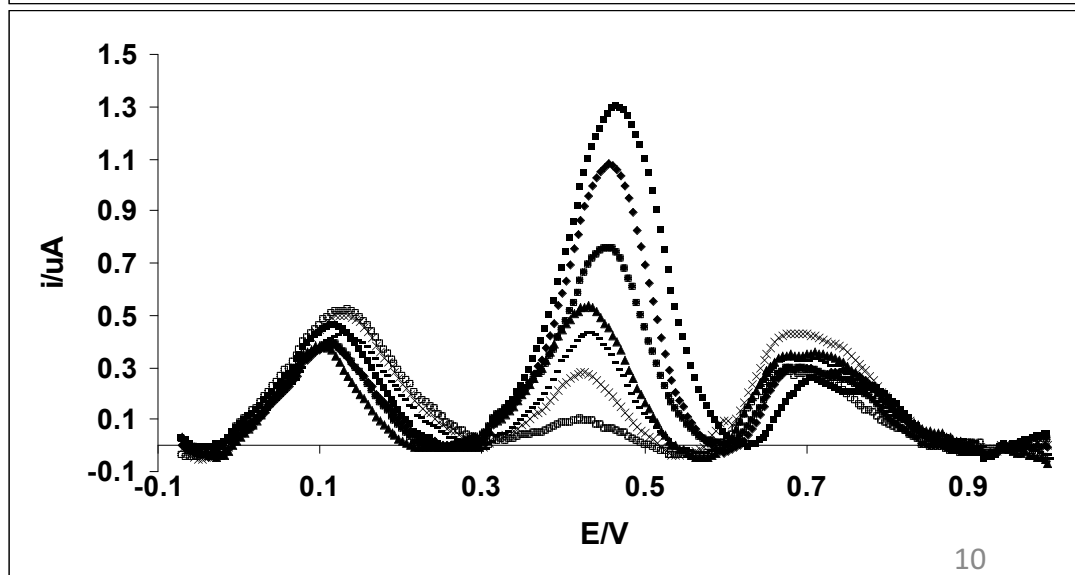
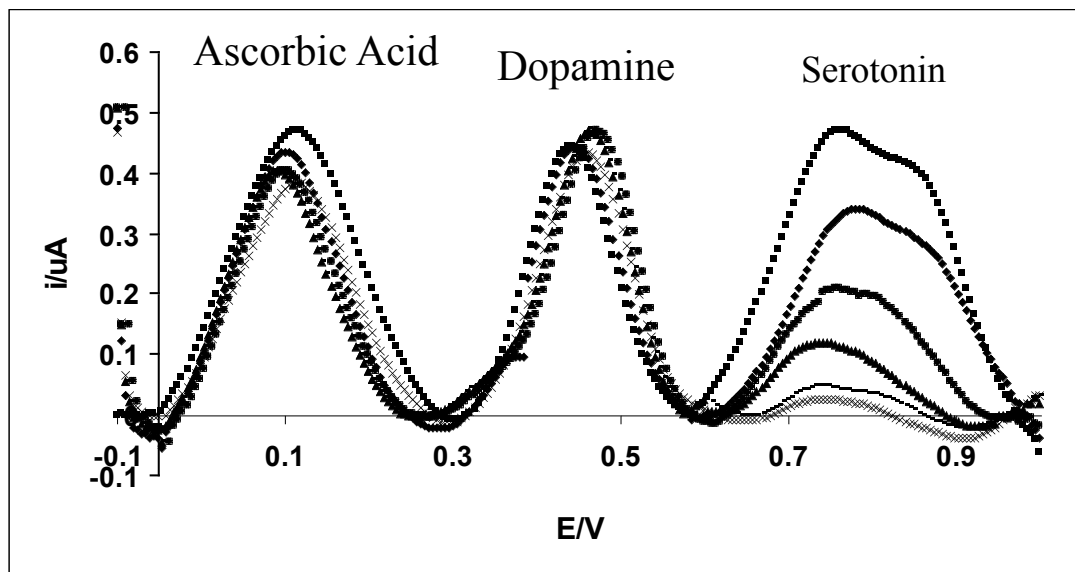
- Molecules of Interest
 - Dopamine
 - Movement disorders, addiction
 - Serotonin
 - Depression, hunger
 - Adenosine
 - Oxygen
 - pH
- Techniques
 - Differential Pulse Voltammetry
 - More sensitive
 - Fast Scan Cyclic Voltammetry
 - Better temporal resolution

Simultaneous Detection of Neurotransmitters

Glassy Carbon Electrode



Carbon Nanofiber Electrode



- CNF electrode has ability to distinguish multiple electroactive brain chemicals in a mixture!
- Detection limits 50nM for DA and 100nM for 5-HT

E. Rand, A. Periyakaruupan, Z. Tanaka, D. A. Zhang, M. P. Marsh, R. J. Andrews, B. Chen, M. Meyyappan, K. H. Lee, J. E. Koehne *Biosens Bioelect* **2013**, 42, 434-438.

Wireless Instantaneous Neurotransmitter Concentration Sensor (WINCS)



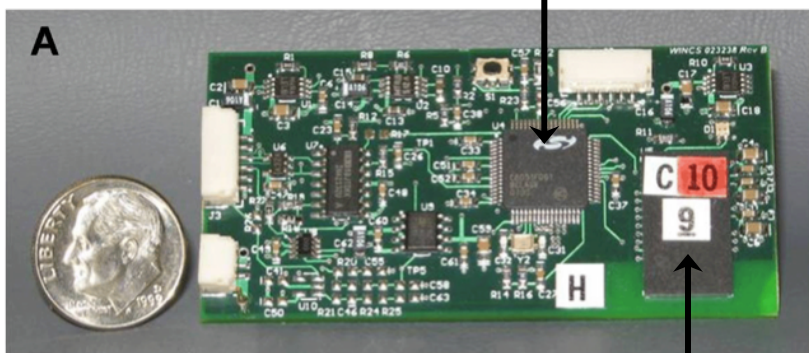
The Mayo Clinic-developed WINCS is a microprocessor-controlled, MRI-compatible, battery-powered instrument that combines Bluetooth® digital telemetry with fast scan cyclic voltammetry and constant potential amperometry.

Standard Potentiostat



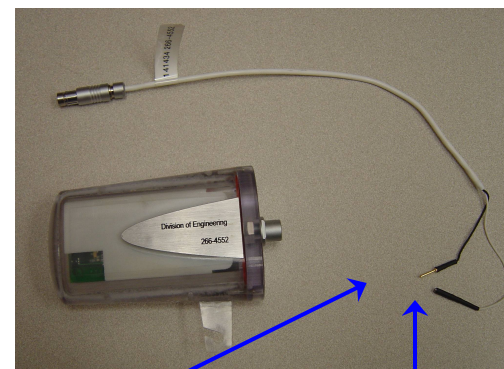
Printed Circuit Board

Microprocessor



Bluetooth®

Sterilizable WINCS Unit



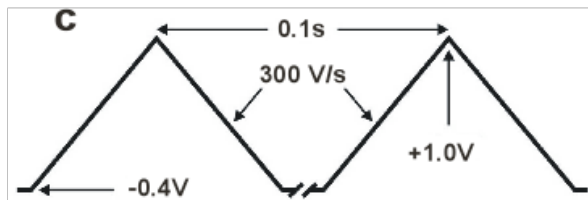
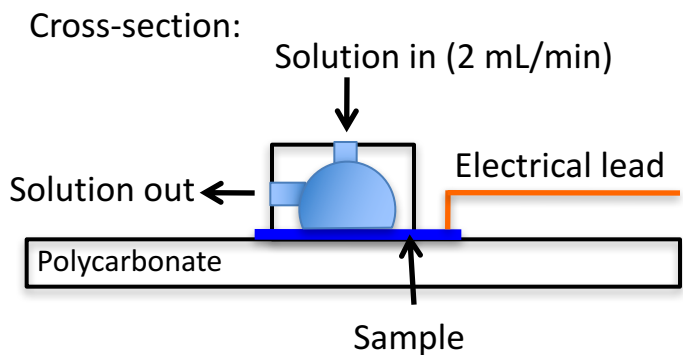
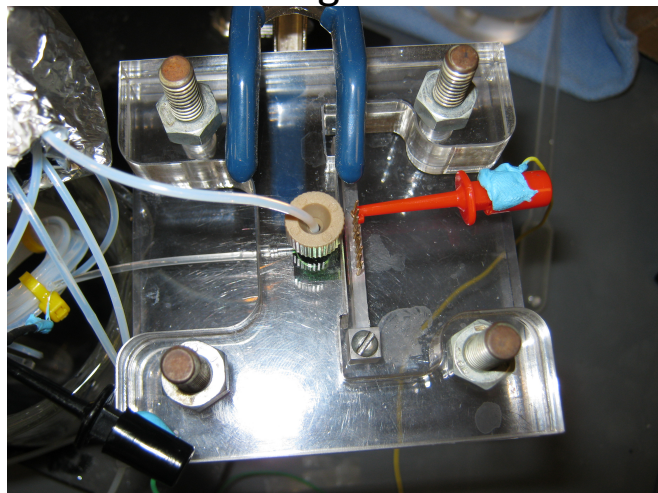
Reference Electrode Lead

Working Electrode Lead

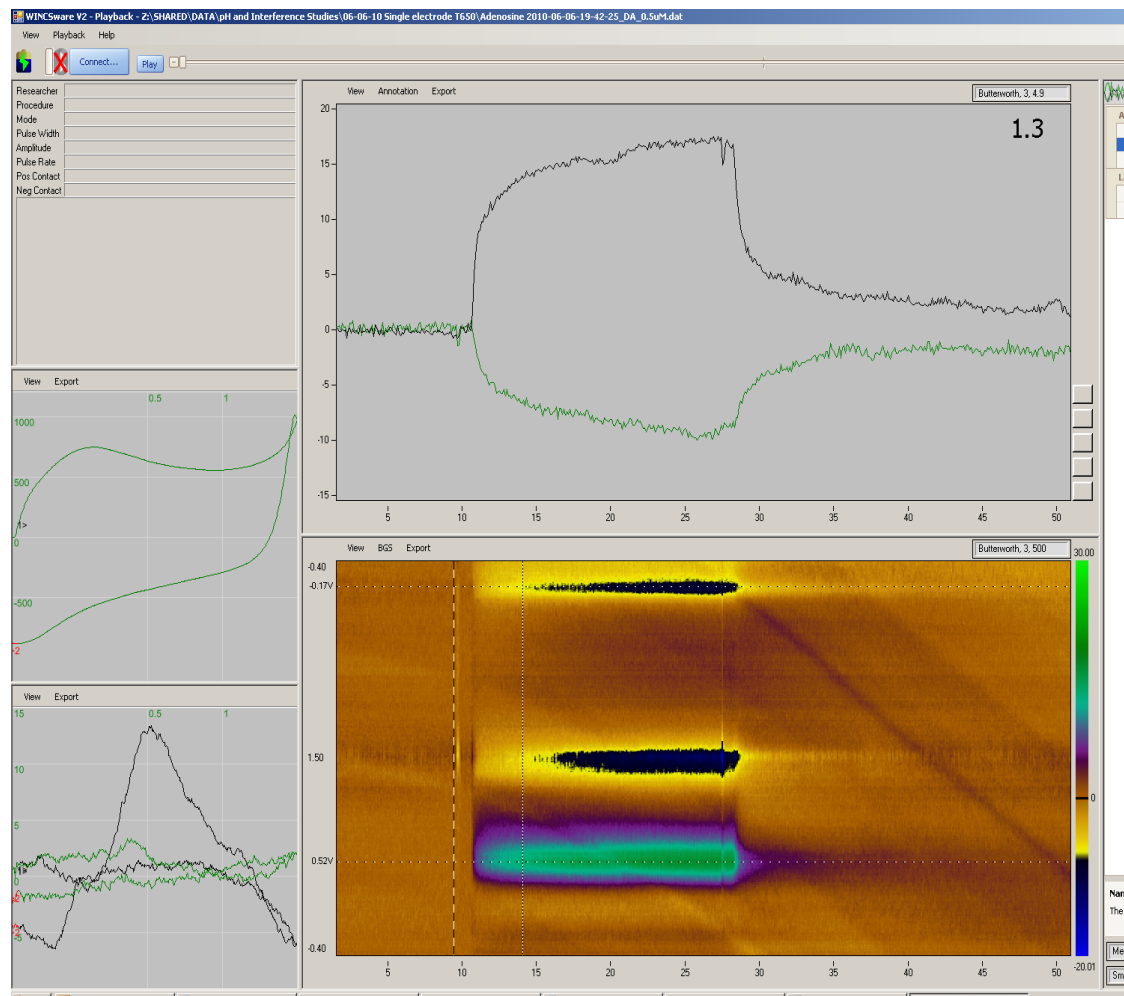
WINCS was designed in compliance with FDA-recognized standards for medical electrical device safety.

Experimental Setup

Custom-Designed Flow Cell

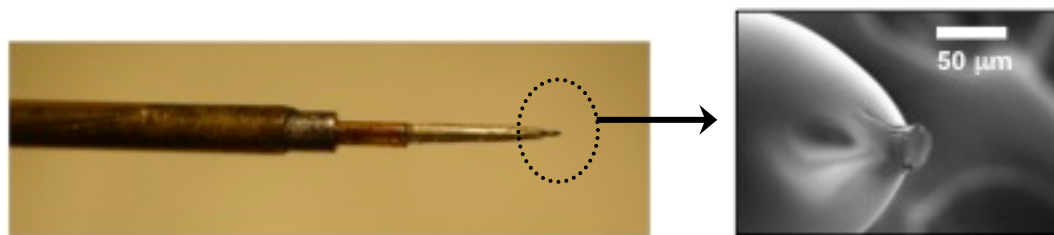


WINCSware User Interface



WINCSware allows viewing of the data in nearly real-time

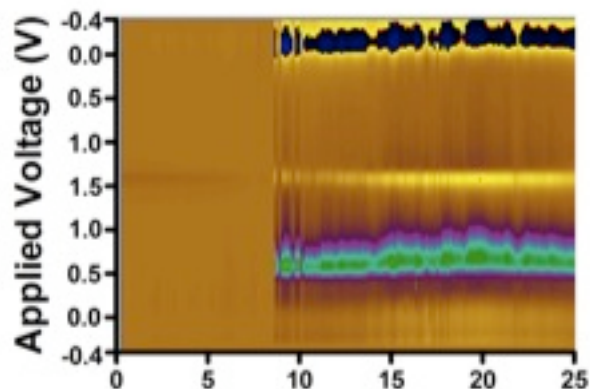
WINCStroke for the Detection of Dopamine



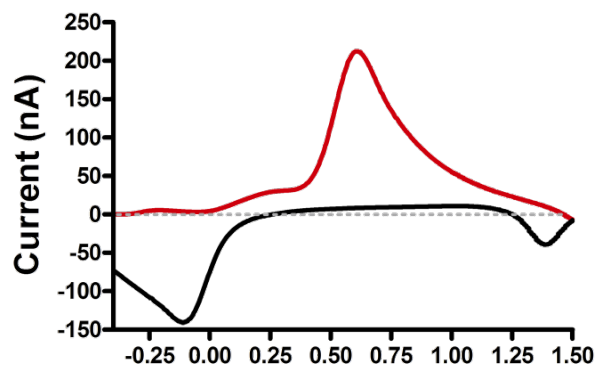
The WINCS carbon fiber electrode (WINCStroke) is based on an approved human extracellular tungsten electrophysiology electrode that was modified by the addition of a short section of carbon-fiber to enable FSCV recordings.

Dopamine Detection:

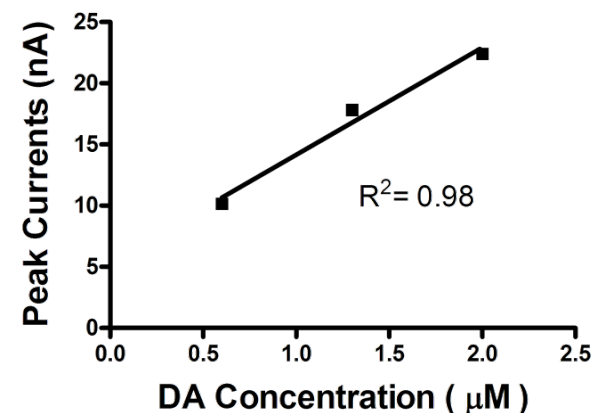
3D Color Plots



Background Subtracted Cyclic Voltammogram

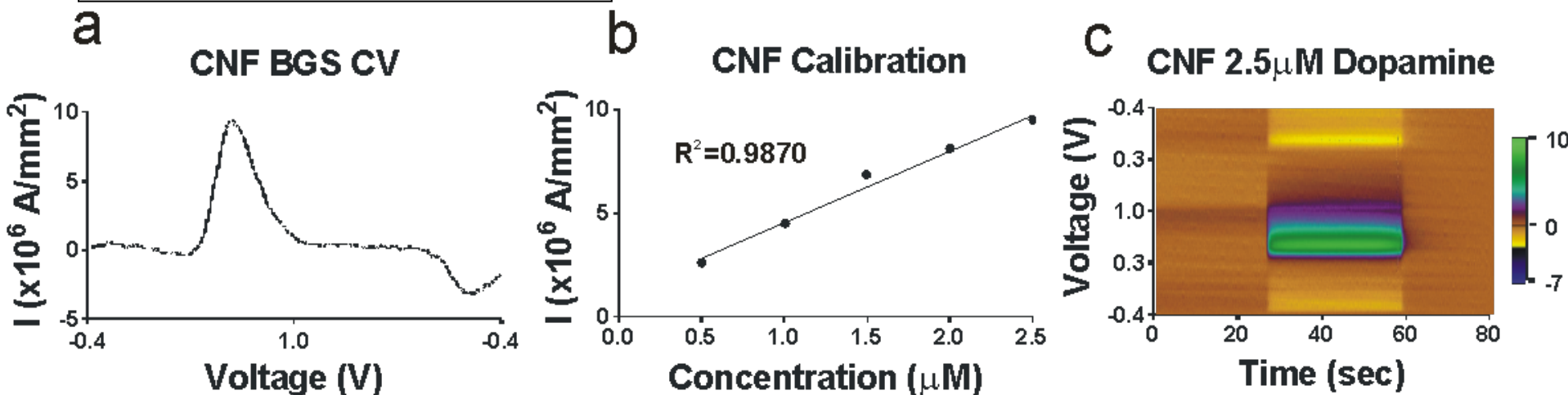


Calibration Curve

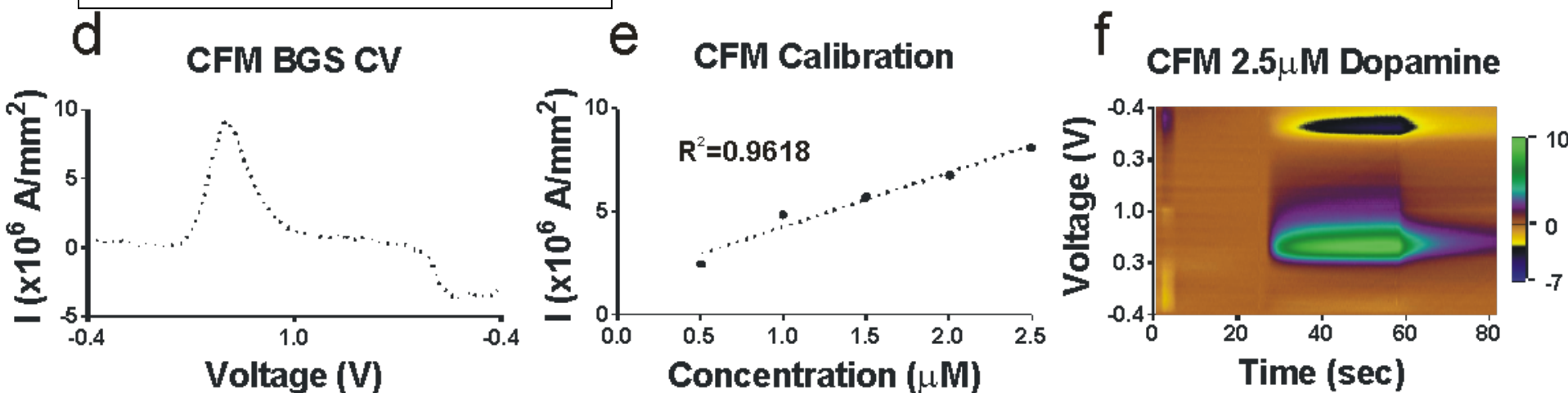


Dopamine Detection

Carbon Nanofiber Electrode

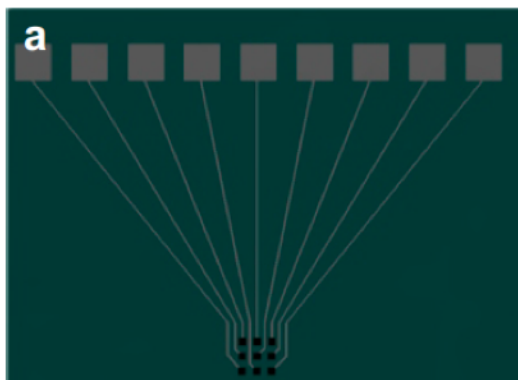


Carbon Fiber Microelectrode

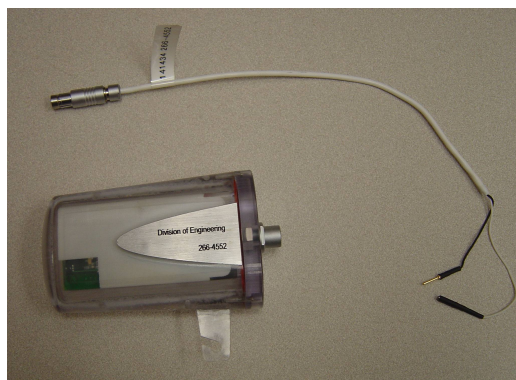


Multichannel Recording

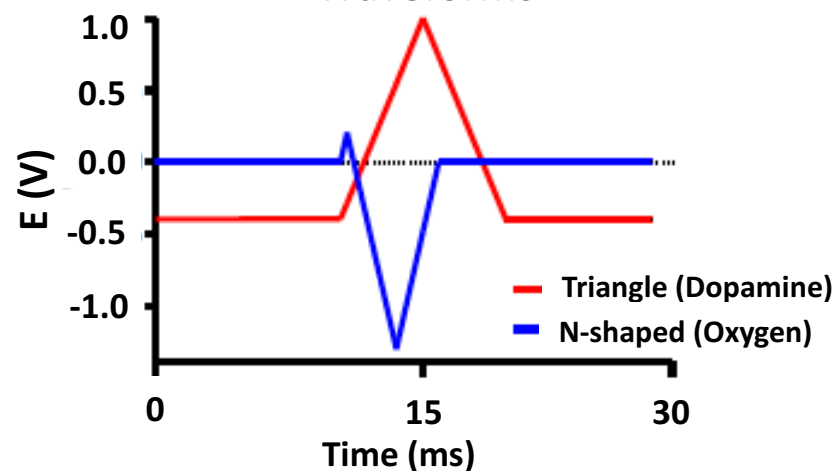
Device: 3x3 Array



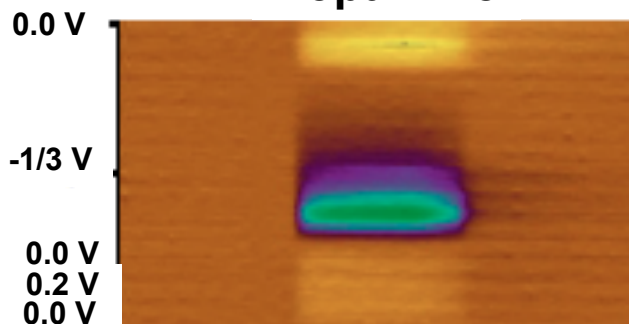
Instruments: 2 WINCS



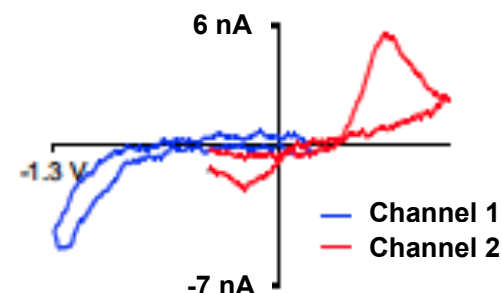
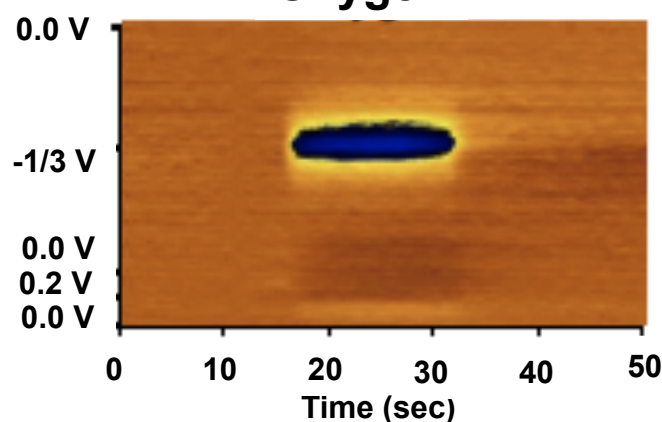
Waveforms



Dopamine

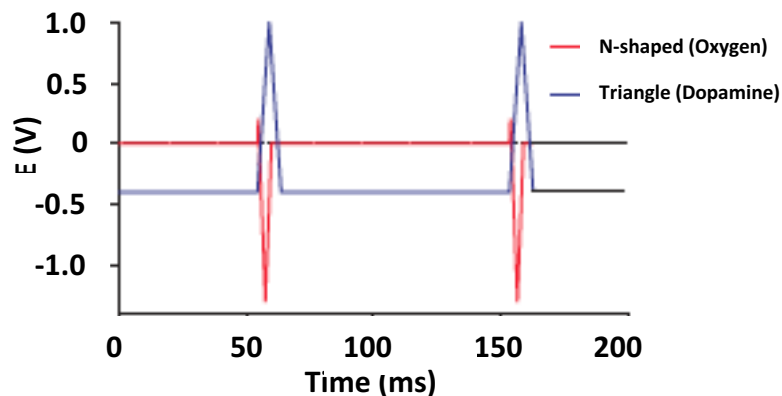


Oxygen

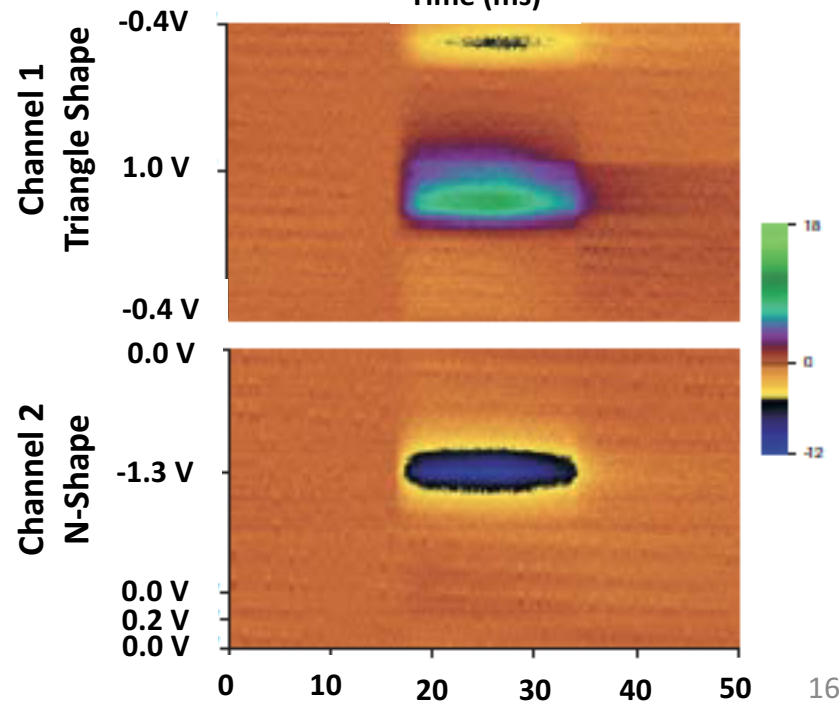
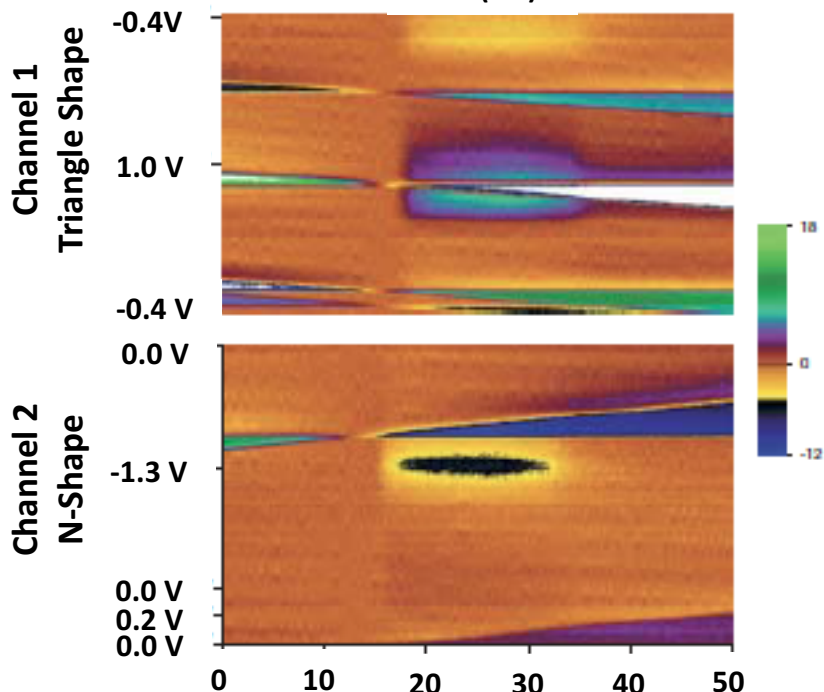
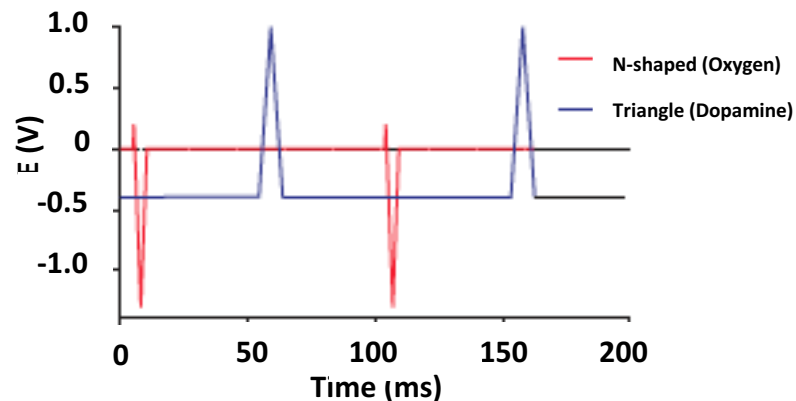


Multichannel Crosstalk

Overlapped Waveforms



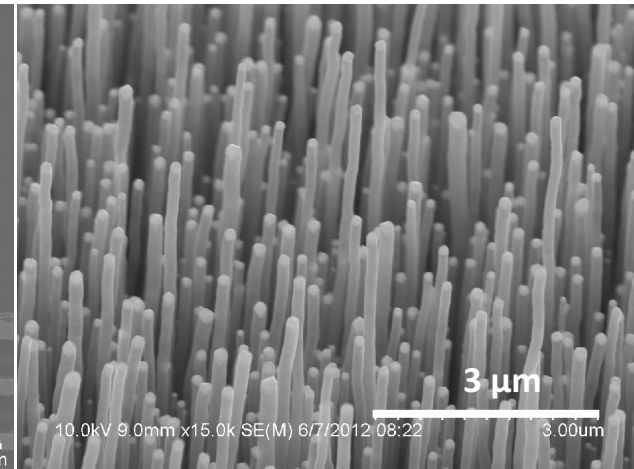
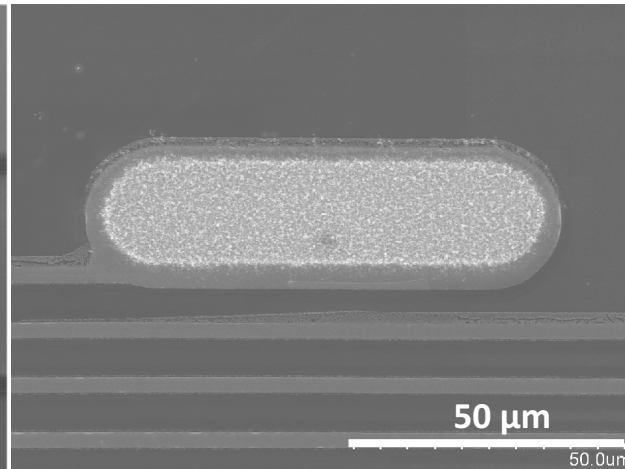
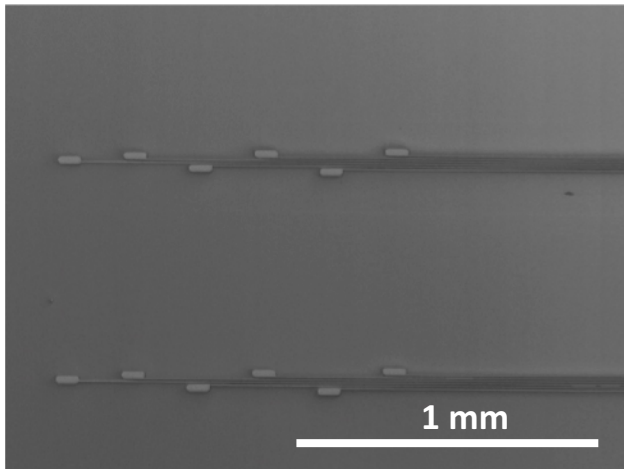
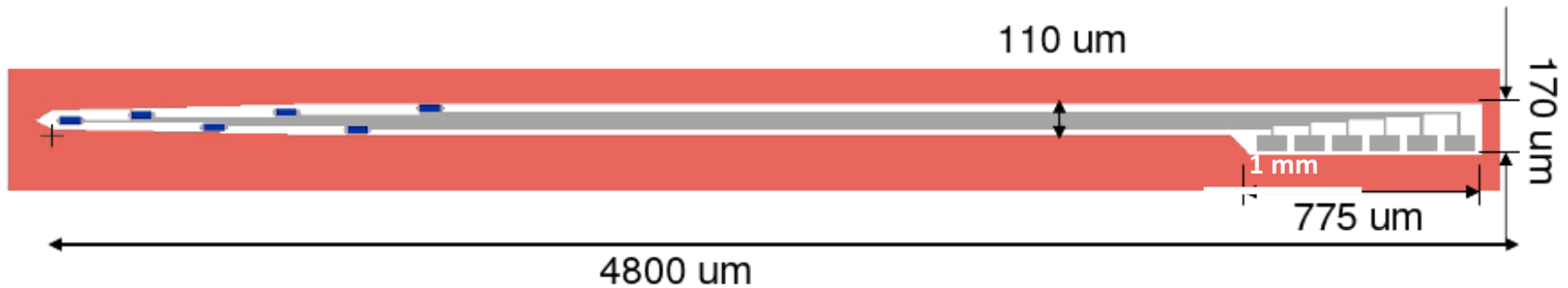
Interleaved Waveforms



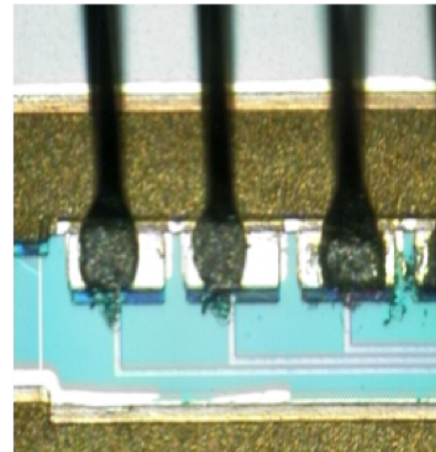
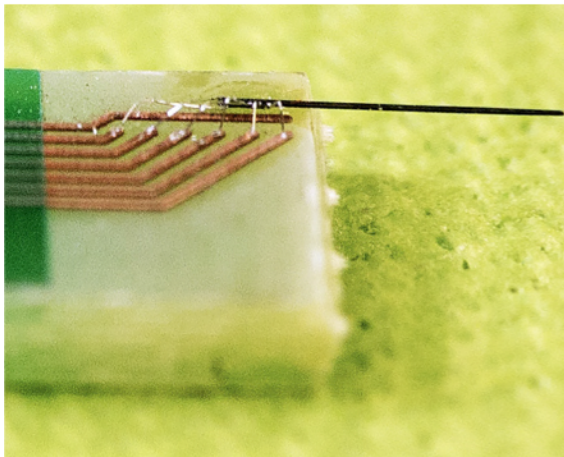
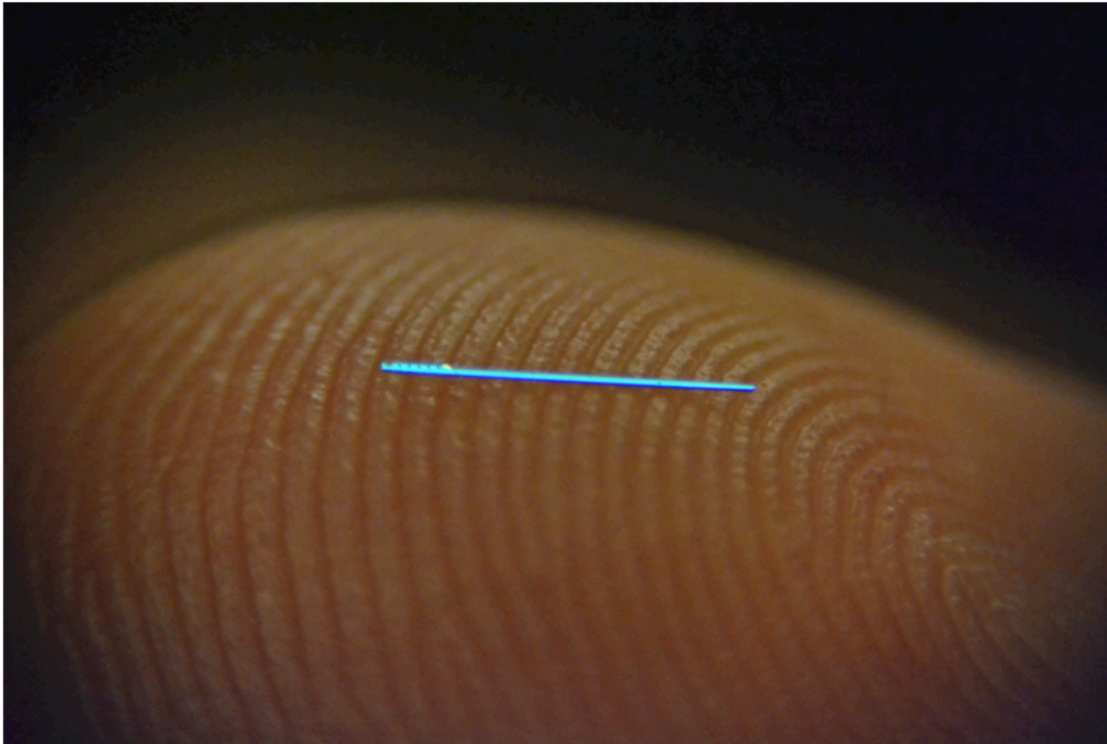
Implantable Style CNF Electrode Needle

Penetrating multiplexed array

- Ability to spatially resolve

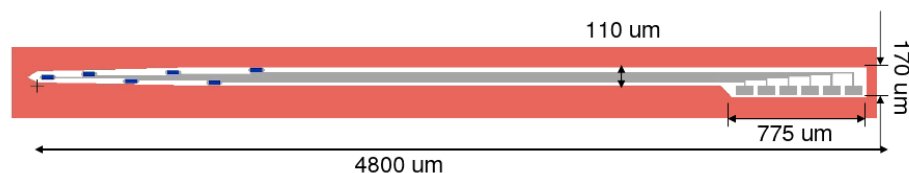


Needle Assembly

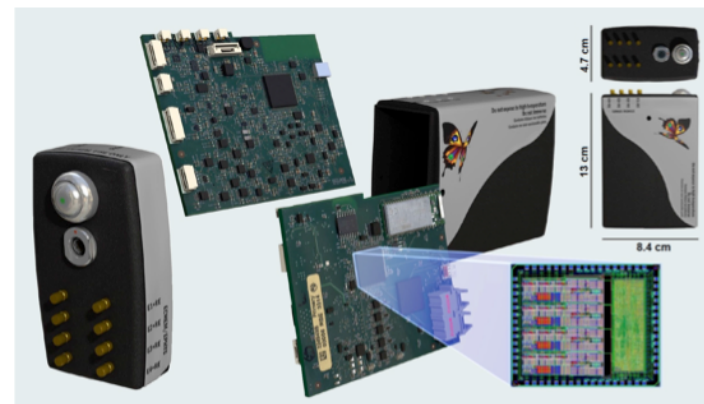


Simultaneous Multichannel Oxygen Detection

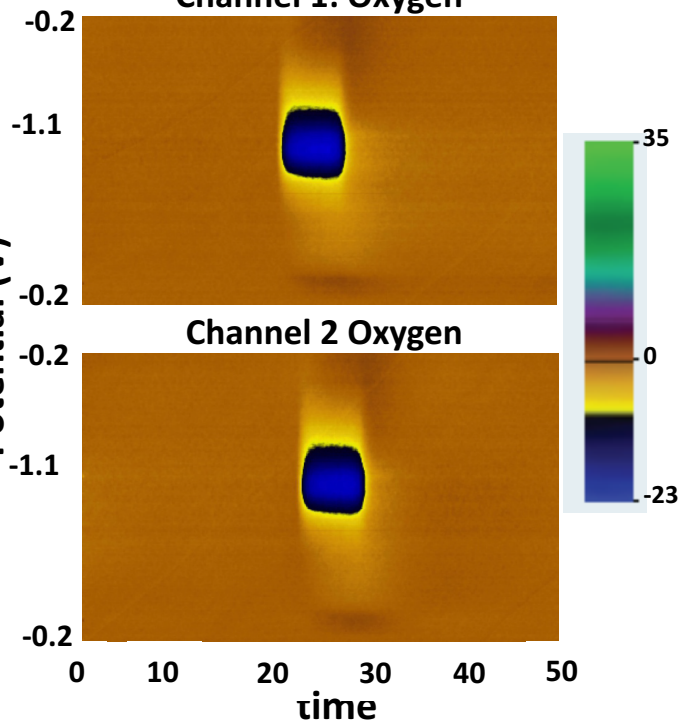
Device: Needle



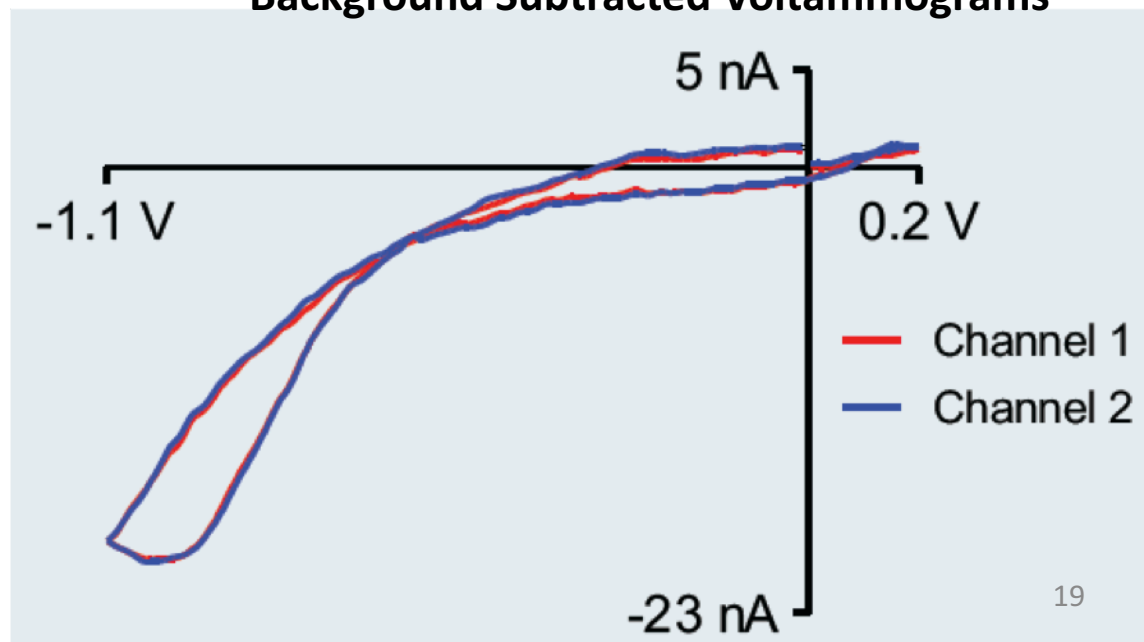
Instrument: WINCS Harmoni



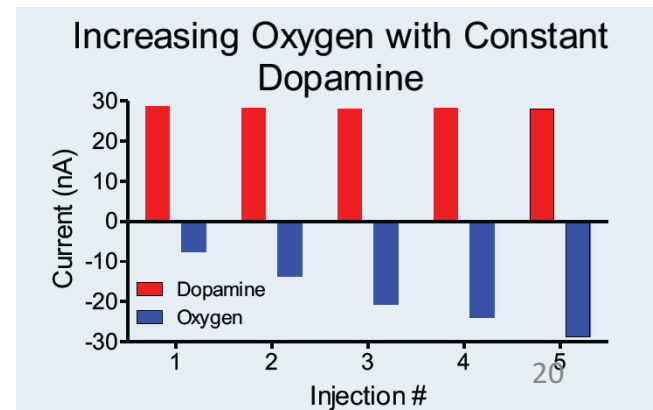
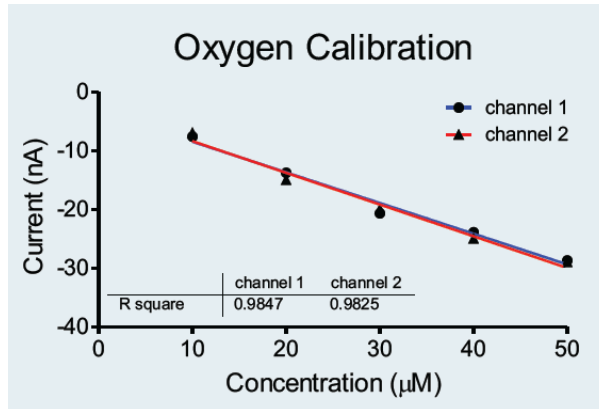
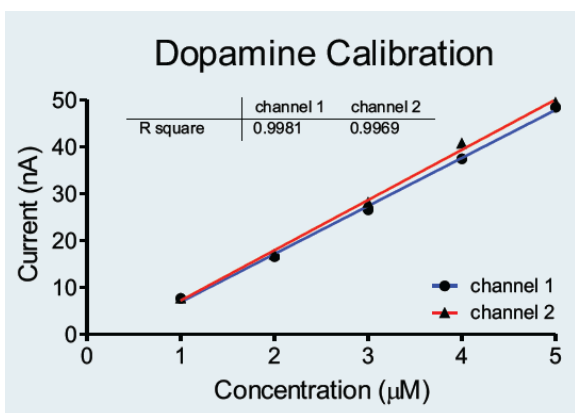
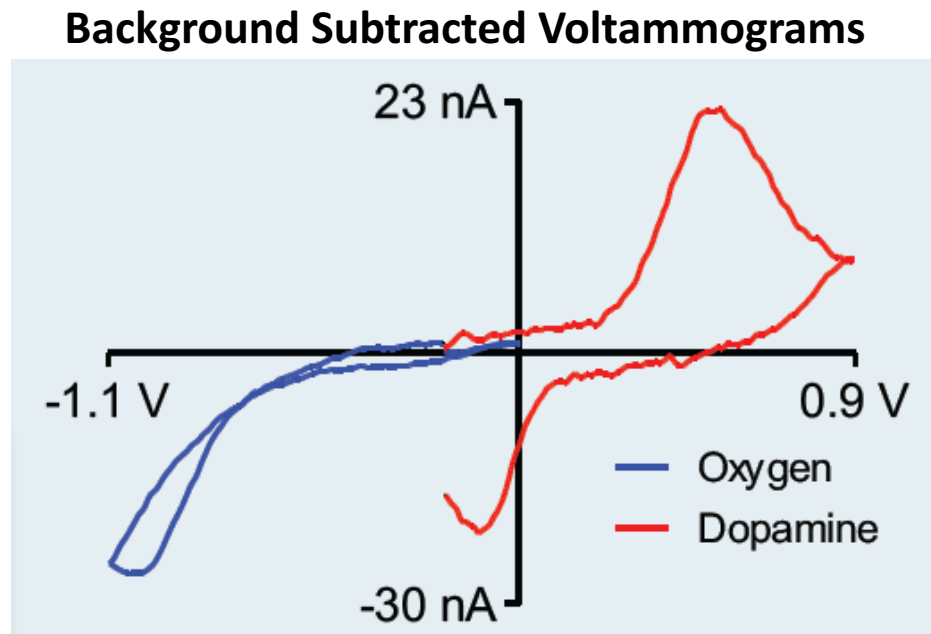
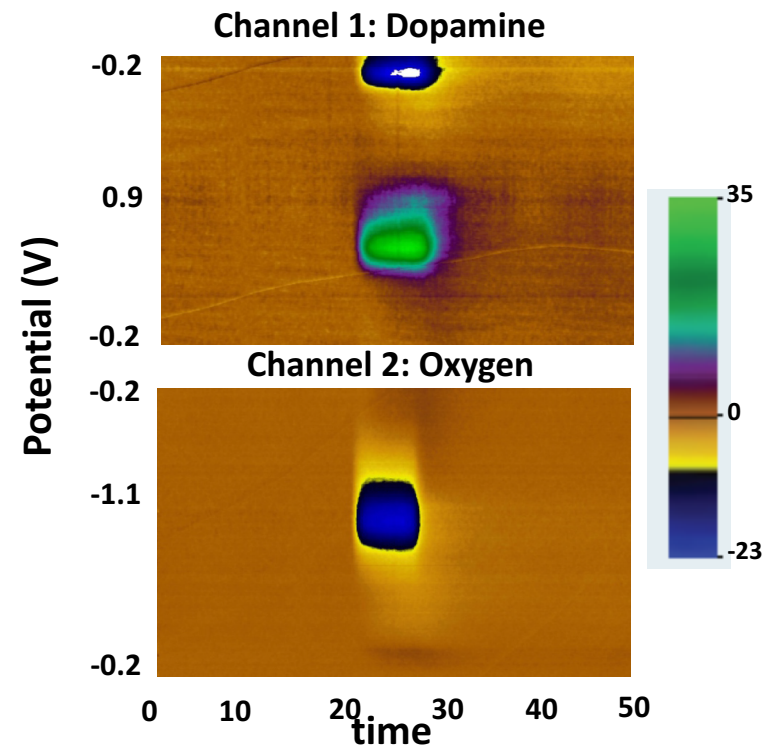
Channel 1: Oxygen



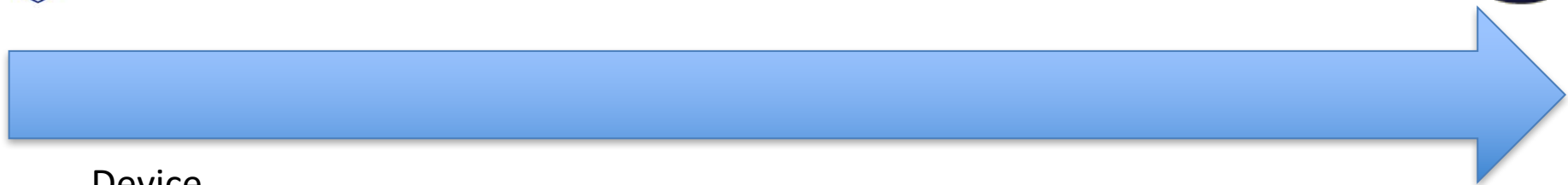
Background Subtracted Voltammograms



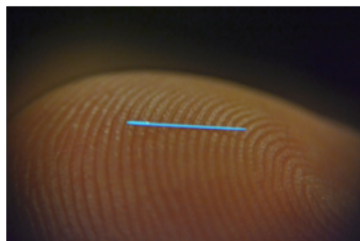
Multichannel Detection: Dopamine and Oxygen



Next Steps



Device



Rat implant
Neurochemical sensing

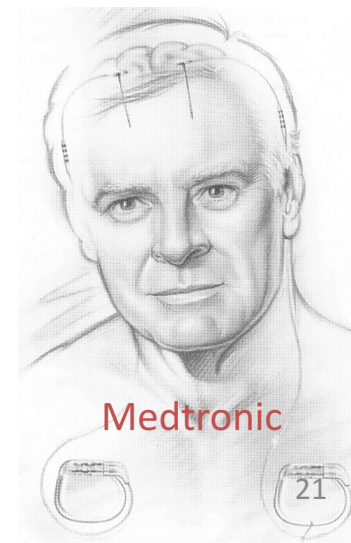


Wikimedia Commons: Vdegroot

Porcine DBS surgery
Stimulation and Sensing



Human Clinical Trial



Summary

- Carbon nanofiber electrode device is well suited for the next generation DBS
 - High sensitivity to act as neurochemical sensing electrodes
- Carbon nanofiber electrode sensors can distinguish between multiple analytes
 - From one electrode using differential pulse voltammetry
 - From adjacent electrodes using fast scan cyclic voltammetry
- Needle style electrode is ready for animal testing

Acknowledgements

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